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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/681,388

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7590 09/19/2007  
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EXAMINER

HISSONG, BRUCE D

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

09/19/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/681,388

Applicant(s)

KENTEN ET AL.

Examiner

Bruce D. Hissong, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 86 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 86 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### **Formal Matters**

1. Applicants response to the office action mailed on 3/9/2007, including arguments/remarks and amendments to the claims, was received on 6/25/2007 and has been entered into the record.

2. Claim 86 is pending and the subject of this office action.

### **Claim Objections**

Claim 86 is objected because it is not clear in part (a)(iii), of the recited C-terminus is the C-terminus of the ubiquitin protein, or of some other protein.

### **Claim Rejections - 35 USC § 112, second paragraph**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Rejection of claim 86 under 35 USC § 112, second paragraph, as being indefinite regarding recitation of "segment[s]" and "group[s]", as set forth on page 3 of the prior office action mailed on 3/9/2007, is withdrawn in response to Applicant's arguments that the double brackets were used to delete the letters, as is permissible under MPEP 714, II, C, (B).

2. Rejection of claim 86 under 35 USC § 112, second paragraph, as being indefinite regarding whether the fusion sites of part (a)(iii) are drawn to the C- or N-terminus, or an internal site, of the ubiquitin protein, or the C- or N-terminus, or an internal site, of some other protein, as set forth on page 3 of the prior office action mailed on 3/9/2007, is withdrawn in response to Applicant's amendments to the claim to the N-terminus "of the ubiquitin protein" and an internal fusion site "of the ubiquitin protein".

**Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Rejection of claim 86 under 35 USC § 102(b) as being anticipated by Vannier *et al*, as set forth on pages 4-5 of the office action mailed on 3/9/2007, is withdrawn in response to Applicants arguments that Vananier *et al* does not teach detection of an ubiquitin-FSHR fusion protein that is non-cleavable. The Applicants cite the teachings of Baker (Curr. Opin. Biotech., 1996, Vol. 7, p. 541-546) as evidence that the fusion protein of Vannier *et al* is non-cleavable. Baker teaches that ubiquitin fusion proteins are readily cleavable except if proline is the amino acid immediately following the ubiquitin moiety (see p. 541, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph; p. 543, 1<sup>st</sup> column, last paragraph). Vannier *et al* has constructed ubiquitin-FSHR fusions wherein ubiquitin is fused to amino acids 23-258 or 172-358 of FSHR. Because neither amino acid 23 or 172 of FSHR is a proline, the resulting fusion protein cannot be non-cleavable.

These arguments have been fully considered and are persuasive.

2. Rejection of claim 86 under 35 USC § 102(b) as being anticipated by Loosfelt *et al*, as set forth on page 5 of the office action mailed on 3/9/2007, is withdrawn in response to Applicants arguments that Loosfelt *et al* does not teach detection of an ubiquitin-TSHR fusion protein that is non-cleavable. The Applicants cite the teachings of Baker (Curr. Opin. Biotech., 1996, Vol. 7, p. 541-546) as evidence that the fusion protein of Loosfelt *et al* is non-cleavable. Baker teaches that ubiquitin fusion proteins are readily cleavable except if proline is the amino acid immediately following the ubiquitin moiety (see p. 541, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph; p. 543, 1<sup>st</sup> column, last paragraph). Loosfelt *et al* has constructed ubiquitin-TSHR fusions wherein ubiquitin is fused to amino acids 19-243 or 604-764 of TSHR. Because neither amino acid 19 or 604 of TSHR is a proline, the resulting fusion protein cannot be non-cleavable.

These arguments have been fully considered and are persuasive.

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**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 86 remain rejected under 35 USC § 103(a) as being obvious in view of either Vannier *et al* or Loosfelt *et al*, as set forth on page 6 of the office action mailed on 3/9/2007.

In the response received on 6/25/2007, the Applicants argue that neither Vannier *et al* nor Loosfelt *et al* teach a fusion protein that meets the limitations of claim 86 because neither reference discloses all elements of the claimed invention. The Applicants also argue that the claimed fusion proteins are not typical of the types used in the art, and at the time of invention, it was not known that non-cleavable fusion proteins would be effective in detection of antibodies because said fusion proteins are constructed with ubiquitin fusion sites not typically used, and/or with proteins not found natively (e.g. with multiple identical epitopes or with non-cleavable epitopes).

These arguments have been fully considered and are not persuasive. The claim, in part (a)(iii), recites a ubiquitin fusion protein comprising ubiquitin fused to a single epitope-containing segment comprising two or more identical or non-identical epitopes, the epitope-containing segment being fused to ubiquitin at fusion sites selected from the group consisting of the C-terminus wherein the fusion site is non-cleavable, the N-terminus of the ubiquitin protein, or an internal fusion site of the ubiquitin protein. Similarly, part (a)(iv) recites a ubiquitin fusion protein comprising ubiquitin fused to a single epitope-containing segment comprising one or more identical or non-identical epitopes, wherein the epitope-containing segment is fused to ubiquitin at the C-terminus wherein said fusion site is non-cleavable, or the N-terminus.

As stated in the previous office action, a person of ordinary skill in the art, guided by the teachings of either Vannier *et al* or Loosfelt *et al*, would know that ubiquitin fusion proteins can be used in methods of detecting antibodies, and thus would have the motivation to create ubiquitin fusion proteins in order to practice such methods. Furthermore, the FSHR moiety of the fusion of Vannier *et al* could be considered to be a single epitope-containing segment, and would be expected to comprise one or more, or two or more, non-identical epitopes. Likewise, the TSHR moiety of the fusion of Loosfelt could also be considered to be a single epitope

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containing segment, and would be expected to comprise one or more, or two or more, non-identical epitopes. It would have been obvious to one of skill in the art at the time of the present invention to optimize the fusion site for the fusion of these single epitope-containing segments comprising one or more non-identical epitopes, and because the only possibilities are fusion at the C-terminus, N-terminus, or internal fusion, one of skill in the art would have both the ability and the motivation to create each possibility in order to create the most immunogenic protein. It is noted that the claims, as currently amended, do not require the fusion at the N-terminus of ubiquitin, or an internal ubiquitin fusion, to be non-cleavable, so one of ordinary skill in the art would also have a reasonable expectation of success in creating a ubiquitin fusion protein comprising the single epitope-containing segment of FSHR or TSHR, as taught by Vannier et al and Loosfelt et al, wherein these segments are fused to ubiquitin at the N-terminus of ubiquitin or fused internally within ubiquitin. When there is motivation to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try may show that it was obvious under § 103 (*KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 82 USPQ2d 1385, 1397 (2007)).

### **Conclusion**

No claim is allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH  
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/Robert S. Landsman/  
Primary Examiner, Art Unit 1647